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PATENT

MAILED BY P.R. Crowley  
DATE 12/17/91

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Daggett et al.		
(PARENT) Serial No.:	08/231,193	Case No.:	SD9383CDB
Filed:	Concurrently Herewith		
Parent	April 20, 1994		
For:	HUMAN N-METHYL-D-ASPARTATE RECEPTOR SUBUNITS, NUCLEIC ACIDS ENCODING SAME AND USES THEREFOR (AS AMENDED)		

Art Unit: 1646

Examiner: Unknown  
Examiner (Parent):  
J. Ulm

The Honorable Assistant Commissioner for Patents  
Washington, D.C. 20231

### PRELIMINARY AMENDMENT

Sir:

This preliminary amendment accompanies a request under 37 CFR § 1.53(b) to file a Divisional application based on Serial No. 09/648,797, filed August 28, 2000, which is a Divisional 08/231,193, filed April 20, 1994. Prior to examination of the application and claims, please amend the application as follows:

### **IN THE SPECIFICATION**

Please amend the specification as follows:

at page 9, lines 1-2, replace "2E, 2F, 2G, 2H, 2I, 2J, 2K, 2L, 2M, 2N, or 2P" with —20, 22, 24, 26, 28, 30, 32, 34, 36, 38 or 40—;

at page 9, line 4, replace "2E, 2F, 2G, 2H, 2I or 2P" with —20, 22, 24, 26, 28, or 40—;

at page 9, lines 9-10, replace "Nos. 1, 1A, 1B, 1C, 1D, 1E, 1F, 1G, 1H, 1I, 1J, 1K, 1L, 1M, 1N, or 1P" with —No. 1, nucleotides 320-3402 of Sequence ID No. 1, or Sequence ID Nos. 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, or 39—;

at page 9, line 14, replace "1E, 1F, 1G, 1H, 1I or 1P" with —19, 21, 23, 25, 27 or 39—;

at page 11, lines 22-23, replace "1E, 1F, 1G, 1H, 1I, 1J, 1K, 1L, 1M, 1N, or 1P" with —19, 21, 23, 25, 27, 29, 31, 33, 35, 37 or 39—;

at page 11, line 25, replace "1E, 1F, 1G, 1H, 1I or 1P" with —19, 21, 23, 25, 27 or 39—;

at page 14, line 19, replace "Sequence ID No. 14." with —Sequence ID No. 56—;

at page 14, line 23, replace "ID No. 13," with —ID No. 55—;

at page 14, line 27, replace "Sequence ID No. 13." with —Sequence ID No. 55—;

at page 14, line 31, replace "6E, 6F, 6G, 6H or 6I" with —46, 48, 50, 52 or 54—;

at page 15, line 3, replace "5A, 5B, 5C, 5D, 5E, 5F, 5G, 5H, or 5I" with —41, 43 or 44 or nucleotides 1-3025 of Sequence ID No. 5 or Sequence ID Nos. 45, 47, 49, 51, or 53—;

at page 15, lines 7-8, replace "5E, 5F, or 5G" with —45, 47, or 49—;

at page 15, line 12, replace "5E, 5F, 5G, 5H or 5I;" with —45, 47, 49, 51 or 53;—;

at page 15, line 14, replace "5E, 5F, or 5G" with —45, 47 or 49—;

at page 15, line 18, replace "Sequence ID No. 16" with —Sequence ID No. 58—;

at page 15, lines 21-22, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 15, line 26, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 15, line 31, replace "SEQ ID Nos. 1, 1A-1P, 5, 5A-5I, 10, 13 or 15" with —Sequence ID No. 1, nucleotides 320-3402 of sequence ID No. 1, Sequence ID Nos. 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 5, 41, 43 or 44, nucleotides 1-3025 of Sequence ID No. 5 or Sequence ID Nos. 45, 47, 49, 51, 53, 10, 55 or 57—;

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at page 16, line 8, replace "SEQ ID Nos. 1, 1A-1P, 5, 5A-5I, 10, 13 or 15." with —Sequence ID No. 1, nucleotides 320-3402 of sequence ID No. 1, Sequence ID Nos. 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 5, 41, 43 or 44, nucleotides 1-3025 of Sequence ID No. 5 or Sequence ID Nos. 45, 47, 49, 51, 53, 10, 55 or 57.—;

at page 37, lines 8-9, replace "(see Sequence ID No. 1B for a description of a portion of NMDA11)" with —(see description of Sequence ID No. 13 in Summary of Sequences for a description of a portion of NMDA11)—;

at page 37, line 13, replace "Sequence ID No. 1D" with —Sequence ID No. 17—;

at page 37, line 14, replace "Sequence ID No. 1C" with —Sequence ID No. 15—;

at page 37, lines 14-15, replace "(see Sequence ID No. 1A for a description of a portion of NMDA10)" with —(which encodes a 3083 nucleotide sequence comprising nucleotides 320-3402 of Sequence ID No. 1)—;

at page 47, line 5, replace "ID. N. 1" with —ID No. 1—;

at page 48, line 11, replace "Sequence ID No. 1J" with —Sequence ID No. 29—;

at page 48, line 12, replace "Sequence ID No. 1K" with —Sequence ID No. 31—;

at page 48, line 13, replace "Sequence ID No. 1M" with —Sequence ID No. 35—;

at page 48, line 14, replace "Sequence ID No. 1N" with —Sequence ID No. 37—;

at page 48, line 15, replace "Sequence ID No. 1L" with —Sequence ID No. 33—;

at page 50, line 31, replace "Sequence ID No. 5D" with —nucleotides 1-3025 of Sequence ID No. 5—;

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at page 50, line 33, replace "ID No. 5C" with —ID No. 44—;

at page 51, line 1, replace "ID No. 5B" with —ID No. 43—;

at page 51, line 2, replace "Sequence ID No. 5A" with —Sequence ID No. 41—;

at page 53, line 14, replace "Sequence ID No. 5E" with —Sequence ID No. 45—;

at page 53, line 18, replace "Sequence ID No. 5F" with —Sequence ID No. 47—;

at page 53, lines 22-23, replace "Sequence ID No. 5G" with —Sequence ID No. 49—;

at page 53, line 25, replace "Sequence ID No. 5H" with —Sequence ID No. 51—;

at page 54, line 1, replace "Sequence ID No. 5I" with —Sequence ID No. 53—;

at page 54, line 23, replace "Sequence ID No. 17" with —Sequence ID No. 59—;

at page 54, line 24, at the beginning of the line, replace "Sequence ID No. 18" with —Sequence ID No. 60—;

at page 54, line 24, after "SE345" replace "(Sequence ID No. 19)" with —(Sequence ID No. 61)—;

at page 54, line 25, replace "Sequence ID No. 20" with —Sequence ID No. 62—;

at page 55, line 8, replace "Sequence ID Nos. 17 and 18" with —Sequence ID Nos. 59 and 60—;

at page 55, line 10, replace "Sequence ID No. 19" with —Sequence ID No. 61—;

at page 55, line 11, replace "Sequence ID No. 20" with —Sequence ID No. 62—;

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at page 55, line 30, replace "Sequence ID No. 21" with —Sequence ID No. 63—;

at page 60, line 21, replace "Sequence ID No. 13" with —Sequence ID No. 55—;

at page 60, lines 22-23, replace "Sequence ID No. 13" with —Sequence ID No. 55—;

at page 60, line 24, replace "Sequence ID No. 13" with —Sequence ID No. 55—;

at page 61, lines 29-30, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 62, line 13, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 62, line 20, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 62, line 33, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 63, line 17, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 63, line 19, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 63, line 30, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 63, lines 31-32, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 63, line 33, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 80, delete lines 6-8 and replace with —Clone NMDA10 encodes a 3083 nucleotide sequence comprising nucleotides 320-3402 of Sequence ID No. 1. Thus, this sequence encoded by the NMDA10 clone differs—;

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at page 80, line 11, replace "Sequence ID No. 1B" with —Sequence ID No. 13—;

at page 80, line 14, replace "Sequence ID No. 1B" with —Sequence ID No. 13—;

at page 80, line 19, replace "Sequence ID No. 1C" with —Sequence ID No. 15—;

at page 80, line 24, replace "Sequence ID No. 1C" with —Sequence ID No. 15—;

at page 81, line 1, replace "Sequence ID No. 1D" with —Sequence ID No. 17—;

at page 81, line 4, replace "Sequence ID No. 1D" with —Sequence ID No. 17—;

at page 81, line 9, replace "Sequence ID No. 1E" with —Sequence ID No. 19—;

at page 81, line 12, replace "Sequence ID No. 1E" with —Sequence ID No. 19—;

at page 81, line 16, replace "Sequence ID No. 1F" with —Sequence ID No. 21—;

at page 81, line 19, replace "Sequence ID No. 1F" with —Sequence ID No. 21—;

at page 81, line 23, replace "Sequence ID No. 1G" with —Sequence ID No. 23—;

at page 81, line 25, replace "Sequence ID No. 1G" with —Sequence ID No. 23—;

at page 81, line 29, replace "Sequence ID No. 1H" with —Sequence ID No. 25—;

at page 81, line 31, replace "Sequence ID No. 1H" with —Sequence ID No. 25—;

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at page 81, line 31, replace "Sequence ID No. 1G" with —Sequence ID No. 23—;

at page 81, line 32, replace "Sequence ID No. 1H" with —Sequence ID No. 25—;

at page 82, line 3, replace "Sequence ID No. 1I" with —Sequence ID No. 27—;

at page 82, line 5, replace "Sequence ID No. 1I" with —Sequence ID No. 27—;

at page 82, line 5, replace "Sequence ID No. 1H" with —Sequence ID No. 25—;

at page 82, line 6, replace "Sequence ID No. 1I" with —Sequence ID No. 27—;

at page 82, line 9, replace "Sequence ID No. 1J" with —Sequence ID No. 29—;

at page 82, lines 10-11, replace "Sequence ID No. 1J" with —Sequence ID No. 29—;

at page 82, line 11-12, replace "Sequence ID No. 1J" with —Sequence ID No. 29—;

at page 82, line 14, replace "Sequence ID No. 1K" with —Sequence ID No. 31—;

at page 82, line 16, replace "Sequence ID No. 1K" with —Sequence ID No. 31—;

at page 82, line 17, replace "Sequence ID No. 1K" with —Sequence ID No. 31—;

at page 82, line 21, replace "Sequence ID No. 1L" with —Sequence ID No. 33—;

at page 82, line 23, replace "Sequence ID No. 1L" with —Sequence ID No. 33—;

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at page 82, line 24, replace "Sequence ID No. 1L" with —Sequence ID No. 33—;

at page 82, line 28, replace "Sequence ID No. 1M" with —Sequence ID No. 35—;

at page 82, line 30, replace "Sequence ID No. 1M" with —Sequence ID No. 35—;

at page 82, line 30, replace "Sequence ID No. 1G" with —Sequence ID No. 23—;

at page 82, line 31, replace "Sequence ID No. 1M" with —Sequence ID No. 35—;

at page 83, line 1, replace "Sequence ID No. 1N" with —Sequence ID No. 37—;

at page 83, line 3, replace "Sequence No. 1N" with —Sequence ID No. 37—;

at page 83, line 3, replace "Sequence ID No. 1G" with —Sequence ID No. 23—;

at page 83, line 4, replace "Sequence No. 1N" with —Sequence ID No. 37—;

at page 83, line 6, replace "Sequence No. 1P" with —Sequence ID No. 39—;

at page 83, line 8, replace "Sequence No. 1P" with —Sequence ID No. 39—;

at page 83, line 8, replace "Sequence ID No. 1H" with —Sequence ID No. 25—;

at page 83, line 9, replace "Sequence No. 1P" with —Sequence ID No. 39—;

at page 83, delete lines 14-16;

at page 83, line 17, replace "Sequence ID No. 2B" with —Sequence ID No. 14—;

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at page 83, line 19, replace "Sequence ID No. 1B" with —Sequence ID No. 13—;

at page 83, line 20, replace "Sequence ID No. 2C" with —Sequence ID No. 16—;

at page 83, line 22, replace "Sequence ID No. 1C" with —Sequence ID No. 15—;

at page 83, line 23, replace "Sequence ID No. 2D" with —Sequence ID No. 18—;

at page 83, line 25, replace "Sequence ID No. 1D" with —Sequence ID No. 17—;

at page 83, line 26, replace "Sequence ID No. 2E" with —Sequence ID No. 20—;

at page 83, line 28, replace "Sequence ID No. 1E" with —Sequence ID No. 19—;

at page 84, line 1, replace "Sequence ID No. 2F" with —Sequence ID No. 22—;

at page 84, line 3, replace "Sequence ID No. 1F" with —Sequence ID No. 21—;

at page 84, line 4, replace "Sequence ID No. 2G" with —Sequence ID No. 24—;

at page 84, line 6, replace "Sequence ID No. 1G" with —Sequence ID No. —23;

at page 84, line 7, replace "Sequence ID No. 2H" with —Sequence ID No. 26—;

at page 84, line 9, replace "Sequence ID No. 1H" with —Sequence ID No. 25—;

at page 84, line 10, replace "Sequence ID No. 2I" with —Sequence ID No. 28—;

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at page 85, line 13, replace "Sequence ID No. 5A" with —Sequence ID No. 41—;

at page 85, line 16, replace "Sequence ID No. 5A" with —Sequence ID No. 41—;

at page 85, line 20, replace "Sequence ID No. 5B" with —Sequence ID No. 43—;

at page 85, line 25, replace "Sequence ID No. 5B" with —Sequence ID No. 43—;

at page 86, line 1, replace "Sequence ID No. 5C" with —Sequence ID No. 44—;

at page 86, line 7, replace "Sequence ID No. 5C" with —Sequence ID No. 44—;

at page 86, delete lines 14-16 and replace with —Nucleotides 1-3025 of Sequence ID No. 5 are a 3025 nucleotide sequence encoded by clone NMDA26. Thus, this sequence differs from—;

at page 86, line 19, replace "Sequence ID No. 5E" with —Sequence ID No. 45—;

at page 86, line 24, replace "Sequence ID No. 5F" with —Sequence ID No. 47—;

at page 86, line 28, replace "Sequence ID No. 5G" with —Sequence ID No. 49—;

at page 87, line 1, replace "Sequence ID No. 5H" with —Sequence ID No. 51—;

at page 87, line 3, replace "Sequence ID No. 5H" with —Sequence ID No. 51—;

at page 87, line 3, replace "Sequence ID No. 5F" with —Sequence ID No. 47—;

at page 87, line 4, replace "Sequence ID No. 5H" with —Sequence ID No. 51—;

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at page 87, line 8, replace "Sequence ID No. 5I" with —Sequence ID No. 53—;

at page 87, line 10, replace "Sequence ID No. 5I" with —Sequence ID No. 53—;

at page 87, line 10, replace "Sequence ID No. 5G" with —Sequence ID No. 49—;

at page 87, line 11, replace "Sequence ID No. 5I" with —Sequence ID No. 53—;

at page 87, line 16, replace "Sequence ID No. 6A" with —Sequence ID No. 42—;

at page 87, line 18, replace "Sequence ID No. 5A" with —Sequence ID No. 41—;

at page 87, line 19, replace "Sequence ID No. 6B is the" with —The—;

at page 87, line 21, replace "Sequence ID No. 5B." with —Sequence ID No. 43 is set forth in Sequence ID No. 43.—;

at page 87, line 22, replace "Sequence ID No. 6C is the" with —The—;

at page 87, line 24, replace "Sequence ID No. 5C." with —Sequence ID No. 44 is set forth in Sequence ID No. 44.—;

at page 87, delete lines 25-27;

at page 87, line 28, replace "Sequence ID No. 6E" with —Sequence ID No. 46—;

at page 87, line 30, replace "Sequence ID No. 5E" with —Sequence ID No. 45—;

at page 88, line 1, replace "Sequence ID No. 6F" with —Sequence ID No. 48—;

at page 88, line 3, replace "Sequence ID No. 5F" with —Sequence ID No. 47—;

at page 88, line 4, replace "Sequence ID No. 6G" with —Sequence ID No. 50—;

10007747-120701

at page 88, line 6, replace "Sequence ID No. 5G" with —Sequence ID No. 49—;

at page 88, line 7, replace "Sequence ID No. 6H" with —Sequence ID No. 52—;

at page 88, line 9, replace "Sequence ID No. 5H" with —Sequence ID No. 51—;

at page 88, line 10, replace "Sequence ID No. 6I" with —Sequence ID No. 54—;

at page 88, line 12, replace "Sequence ID No. 5I" with —Sequence ID No. 53—;

at page 88, line 15, replace "5C, 5E and 5H." with —44, 45 and 51.—;

at page 88, line 25, replace "5B and 5C." with —43 and 44.—;

at page 89, line 8, replace "Sequence ID No. 13" with —Sequence ID No. 55—;

at page 89, line 11, replace "Sequence ID No. 14" with —Sequence ID No. 56—;

at page 89, line 12, replace "Sequence ID No. 13" with —Sequence ID No. 55—;

at page 89, line 13, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 89, line 16, replace "Sequence ID No. 16" with —Sequence ID No. 58—;

at page 89, line 17, replace "Sequence ID No. 15" with —Sequence ID No. 57—;

at page 89, line 18, replace "Sequence ID Nos. 17-20" with —Sequence ID Nos. 59-62—; and

at page 89, line 22, replace "Sequence ID No. 21" with —Sequence ID No. 63—.

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**IN THE CLAIMS**

Please cancel claims 1-36 and insert in place thereof the following new claims:

37. An isolated and substantially pure receptor encoded by a DNA sequence, comprising a sequence of nucleotides that encode an human N-methyl-D-aspartate receptor subtype, wherein said sequence of nucleotides is set forth in SEQ ID No. 57.
38. A substantially pure human N-methyl-D-aspartate receptor subtype comprising the sequence of amino acids as set forth in SEQ ID No. 58.
39. The receptor according to claim 37, where the receptor is an human N-methyl-D-aspartate receptor type 2D subunit (NMDAR2D).
40. A method for detecting a binding partner for the receptor of claim 37 in a sample suspected of containing the binding partner, comprising:
- (i) contacting the sample with the receptor under conditions favoring binding of the receptor to the binding partner;
  - (ii) determining presence of the binding partner in the sample by detecting binding of the receptor to the binding partner.
41. A method of identifying a polypeptide which is active in a signal transduction pathway of a cell of which the receptor of claim 37 is a component, said method comprising:
- (a) contacting a cell extract suspected of containing the polypeptide with an antibody that specifically binds to the polypeptide under conditions favoring formation of an antibody/polypeptide complex,
  - (b) identifying the antibody/polypeptide complex, and
  - (c) assaying the complex obtained in (b) to identify any polypeptide bound to the polypeptide other than the antibody.

42. A method for screening for the presence of a neurological disorder, comprising assaying a tissue from a subject to determine level of expression of the receptor according to claim 37, wherein increased or reduced level of the receptor compared to a normal level is an indication that the subject is at risk of developing the neurological disorder.
43. A method for following progress of a therapeutic régime designed to alleviate a condition characterized by abnormal expression of the receptor of claim 37, comprising:
- (a) assaying a sample from a subject to determine level of a parameter selected from the group consisting of (i) a receptor encoded by the nucleotide sequence of SEQ. ID. NO. 57 and (ii) a receptor having the amino acid sequence as set forth in SEQ. ID. NO. 58, at a first time point;
  - (b) assaying level of the parameter selected in (a) at a second time point and
  - (c) comparing the level at the second time point to the level determined in (a) as a determination of effect of the therapeutic régime.
44. A host cell transformed with a nucleic acid molecule that encodes the polypeptide of claim 37.
45. An antibody that is specifically binds to the polypeptide of claims 37.

#### STATUS OF CLAIMS:

Claims 1-36 were pending.

New claims 37- 45 are added herein.

Claims 37 - 45 are presented for consideration.

**REMARKS**

By this amendment, Applicants have canceled original claims 1-36 and inserted in place thereof new claims 37-45. The new claims are designed to conform to a Restriction requirement set forth in the parent application Serial No. 08/231,193 and in application Serial No. 09/648,797, which is a Divisional Application of the parent application. Hence no new matter is added.

It is believed that the instant claims contain patentable subject matter and a notice to that effect is earnestly solicited.

Any fees that may be due in connection with the filing of this paper of application may be charged to Deposit Account No. 13-2755.

If the Examiner believes that a telephone conference would be of value, he is requested to call the undersigned counsel at the number listed below.

Respectfully submitted,

By 

Vineet Kohli

Reg. No. 37,003

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Date: December 7, 2001